The immunology of neurodegeneration.

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Public Summary:
The ability of the adult brain to generate newly born neurons dramatically declines during aging, and has even been proposed to contribute, in part, to age-related cognitive impairments. While intrinsic molecular mechanisms underlying decreased neurogenesis during aging have begun to be elucidated, relatively little is still known as to the contribution of the systemic environment. Interestingly, immune signaling has quickly emerged as a key negative regulator of adult neurogenesis, and has more recently been functionally linked to the aging circulatory systemic environment. In this review we examine the role of the aging systemic environment in regulating adult neurogenesis and cognitive function. We discuss recent work from our group using the aging model of heterochronic parabiosis - in which the circulatory system of two animals is connected - to highlight the contribution of circulatory immune factors to age-related impairments in adult neurogenesis and associated cognitive processes. Finally, we propose the possibility of combating brain aging by tapping into the 'rejuvenating' potential inherent in a young circulatory systemic environment.

Scientific Abstract:
While immune responses in neurodegeneration were regarded as little more than a curiosity a decade ago, they are now increasingly moving toward center stage. Factors driving this movement include the recognition that most of the relevant immune molecules are produced within the brain, that microglia are proficient immune cells shaping neuronal circuitry and fate, and that systemic immune responses affect brain function. We will review this complex field from the perspective of neurons, extra-neuronal brain cells, and the systemic environment and highlight the possibility that cell intrinsic innate immune molecules in neurons may function in neurodegenerative processes.